[0028] FIG. **4** illustrates a result of measuring the cumulative number of viable cells during a culture period.

DESCRIPTION OF THE PREFERRED EMBODIMENTS

[0029] Hereinafter, embodiments for carrying out an aspect of the present invention will be described in detail.

[0030] In the present specification, a numerical value range indicated by using "to" means a range including numerical values described before and after the "to" as a minimum value and a maximum value, respectively.

[0031] [Animal Cells]

[0032] An animal cell of an aspect of the present invention is an animal cell that includes a gene encoding a target protein and a foreign gene encoding SNAT2 and linked to a promoter, and overexpresses the SNAT2.

[0033] The expression of the SNAT2 gene activates the mTORC1/S6K pathway in a mouse liver (Nature Communications 6, Article number: 7940 (2015)), and this thus suggests a relationship between the expression of the SNAT2 gene and the expression of the mTOR gene. It has been reported that in rat cells, cell proliferation is suppressed by activation of mTOR and cell size is increased (Genes Dev. 2002 Jun 15; 16 (12): 1472-1487). In addition, it has also been shown that the larger the cell size, the greater the production amount of a protein product (Cytotechnology 34: 59-70, 2000). However, the relationship between SNAT2 gene expression and the production amount of recombinant protein is unclear.

[0034] In WO2009/020144, a decrease in survival rate was moderated due to the effect of introducing alanine aminotransferase, but since the period that survival rate of cells is 60% or less is long, there is concern about the influence on antibody quality. In addition, since the antibody productivity (Qp) per cell is lowered by the introduction of the taurine transporter, there is a problem that even if the cell density is increased, it does not lead to the production amount. On the other hand, in an aspect of the present invention, antibody productivity (Qp) per cell is improved by enhancing the expression of the SNAT2 gene involved in protein biosynthesis.

[0035] <Target Protein>

[0036] In an aspect of the present invention, the kind of the target protein is not particularly limited, and examples thereof include a recombinant polypeptide chain, a recombinant secreted polypeptide chain, an antigen-binding protein, a human antibody, a humanized antibody, a chimeric antibody, a mouse antibody, a bispecific antibody, and an Fc fusion protein, a fragmented immunoglobulin, and a single-chain antibody (scFv). The target protein is preferably a human antibody, a humanized antibody, a chimeric antibody, or a mouse antibody. Examples of the fragmented immunoglobulin include Fab, $F(ab')_2$, Fv, and the like. The class of the antibody is also not particularly limited, and may be any one class of IgG such as IgG1, IgG2, IgG3, and IgG4, IgA, IgD, IgE, or IgM, but in a case of being used as a medicine, IgG and IgM are preferable.

[0037] Human antibodies include all antibodies having one or a plurality of variable and constant domains introduced from human immunoglobulin sequences. In one embodiment, all of the variable and constant domains are introduced from human immunoglobulin sequences (complete human antibodies).

[0038] The humanized antibody has a sequence different from a sequence of an antibody introduced from a non-human species by substitution, deletion, and/or addition of one or a plurality of amino acids, so that there is a low possibility for the humanized antibody to induce an immune response, and/or so that induction of a severe immune response is reduced, compared to the non-human species antibody, in a case of being administered to a human subject. In one embodiment, specific amino acids in a framework and constant domains of heavy chains and/or light chains of a non-human species antibody are mutated to produce a humanized antibody. In another embodiment, the constant domains of human antibodies are fused to variable domains of a non-human antibodies.

[0039] The chimeric antibody is an antibody in which variable domains and constant domains having different origins from each other are linked. For example, an antibody consisting of variable domains of heavy chains and light chains of a mouse antibody and the constant domains of heavy chains and light chains of a human antibody is a mouse/human heterologous chimeric antibody. It is possible to prepare a recombinant vector expressing a chimeric antibody by linking a DNA encoding the variable domains of a mouse antibody and a DNA encoding the constant domains of a human antibody, and incorporating thereof into an expression vector. It is possible to obtain a chimeric antibody produced during the culture by culturing a recombinant cell transformed with the vector and expressing the incorporated DNA.

[0040] A bispecific antibody is an antibody that recognizes two different antigenic specificities and are prepared by a chemical method or cell fusion. As a method for preparing a bispecific antibody, a method of preparing a bispecific antibody by binding two immunoglobulin molecules by using a cross-linking agent such as N-succinimidyl 3-(2-pyridyldithiol) propionate or S-acetylmercaptosuccinic acid anhydride, a method of preparing a bispecific antibody by binding Fab fragments of immunoglobulin molecules with each other, and the like have been reported.

[0041] An Fc fusion protein indicates a protein having an Fc domain and includes an antibody.

[0042] Fab is a monovalent fragment having V_L, V_H, C_L and C_H1 domains.

[0043] $F(ab')_2$ is a bivalent fragment having two Fab fragments bound by a disulfide cross-linking at a hinge domain.

[0044] The Fv fragment has a single arm V_L and V_H domains of an antibody.

[0045] Single-chain antibody (scFv) is an antibody in which the V_L and V_H domains are joined via a linker (for example, a synthetic sequence of an amino acid residue) to form a continuous protein chain, in which the linker is long enough to fold the protein chain on itself and to form a monovalent antigen binding site.

[0046] A gene encoding a target protein can be obtained by a method known to those skilled in the art. In a case where the target protein is an antibody, it is possible to use a DNA encoding the L chain and a DNA encoding the H chain of the antibody.

[0047] It is possible to prepare the DNA encoding the L chain and the DNA encoding the H chain of the antibody as follows. An mRNA is extracted from a hybridoma, a cell, a phage, a ribosome, or the like having a gene that expresses an antibody. A cDNA is prepared by a reverse transcription